



Prevalence and Characteristics of Dry Eye Disease After Cataract Surgery: A Systematic Review and Meta-Analysis

Maria Miura · Takenori Inomata · Masahiro Nakamura · Jaemyoung Sung · Ken Nagino · Akie Midorikawa-Inomata · Jun Zhu · Keiichi Fujimoto · Yuichi Okumura · Kenta Fujio · Kunihiro Hirosawa · Yasutsugu Akasaki · Mizu Kuwahara · Atsuko Eguchi · Hurramhon Shokirova · Akira Murakami

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ABSTRACT

Dry eye disease (DED) after cataract surgery is associated with various risk factors, while causing a wide range of heterogeneous symptoms including decreased quality of vision. This systematic review and meta-analysis aimed to determine the prevalence and characteristics of DED after cataract surgery. We searched PubMed and EMBASE and included studies on patients with

DED after cataract surgery, between January 2011 and June 2020. Study-specific estimates (DED prevalence rates after cataract surgery in patients without preexisting DED) were combined using one-group meta-analysis in a random-effects model. We included 36 studies published between 2013 and 2020. We included nine of these in the meta-analysis of DED prevalence after cataract surgery. Overall 37.4% (95% CI 22.6–52.3; 206/775) of patients without preexisting DED developed DED after cataract surgery. The risk

M. Miura · T. Inomata (✉) · J. Sung · J. Zhu · K. Fujimoto · Y. Okumura · K. Fujio · K. Hirosawa · Y. Akasaki · M. Kuwahara · H. Shokirova · A. Murakami
Department of Ophthalmology, Juntendo University Graduate School of Medicine, 2-1-1 Hongo, Bunkyo-Ku, Tokyo 113-0033, Japan
e-mail: tinoma@juntendo.ac.jp

M. Miura · T. Inomata · M. Nakamura · K. Fujimoto · Y. Okumura · K. Fujio · K. Hirosawa · Y. Akasaki · M. Kuwahara · A. Murakami
Department of Digital Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan

T. Inomata · A. Murakami
Department of Ophthalmology, Juntendo University Faculty of Medicine, Tokyo, Japan

T. Inomata · Y. Okumura
Department of Strategic Operating Room Management and Improvement, Juntendo University Graduate School of Medicine, Tokyo, Japan

T. Inomata · K. Nagino · A. Midorikawa-Inomata · A. Eguchi
Department of Hospital Administration, Juntendo University Graduate School of Medicine, Tokyo, Japan

M. Nakamura
Department of Bioengineering, Graduate School of Engineering, Precision Health, The University of Tokyo, Tokyo, Japan

J. Zhu
Department of Ophthalmology, Subei People's Hospital Affiliated to Yangzhou University, Yangzhou, Jiangsu Province, China

factors for DED after cataract surgery included age, female sex, systemic diseases, systemic medications, psychiatric conditions, preexisting DED, meibomian gland dysfunction, preservatives in eye drops, surgery techniques, and lifestyle. DED severity peak occurred 1 day postoperatively and persisted for at least 1–12 months following cataract surgery; therefore, consistent follow-up for DED is warranted for at least 1 month after cataract surgery. Topical administration of preservative-free diquafosol tetrasodium solution and preoperative meibomian gland treatment were effective in preventing and treating DED following cataract surgery. As more than one-third of patients develop DED after cataract surgery, careful DED management and treatment is needed after cataract surgery to improve satisfaction and vision quality.

Keywords: Cataract surgery; Characteristics; Dry eye disease; Meta-analysis; Prevalence; Risk factors; Systematic review; DED; MGD; Meibomian gland dysfunction

Key Summary Points

This large-scale systematic review and meta-analysis aimed to comprehensively present dry eye disease (DED) prevalence and its associated risk factors, specifically among patients who have undergone cataract surgery without preexisting DED.

A wide range of data on surgery-specific factors was analyzed (i.e., surgical techniques, postsurgical treatment), which contributed to a broader understanding of DED pathogenesis.

This study identified that 37.4% (95% CI 22.6–52.3; 206/775) of patients without preexisting DED developed DED following cataract surgery.

The timelines of symptom severity according to different measurement intervals and duration were compiled, yielding a more accurate pattern of DED progression following cataract surgery.

A major portion of the included studies were based on the Asian population, which calls for further verification of the generalizability of the results.

INTRODUCTION

Cataract surgery is an increasingly prevalent ophthalmic procedure owing to an aging society [1, 2]. Although it yields excellent results in most patients, some develop postoperative disorders, such as dry eye disease (DED) [3–5], with symptoms including dryness, foreign body sensation, and ocular fatigue [6, 7]. This negatively impacts the quality of vision (QOV) and work productivity and has economic repercussions [8], warranting preventative and management strategies for DED after cataract surgery [9].

The pathogenesis of DED after cataract surgery remains unclear, resulting in a lack of evidence-based, established treatment [9]. Moreover, there have been no systematic or large-scale studies on DED following cataract surgery in individuals without preexisting DED to comprehensively elucidate its risk factors, duration, and treatment.

This systematic review and meta-analysis aimed to summarize the current evidence to identify the prevalence, characteristics, perioperative risk factors, treatment, and preventative measures for DED after cataract surgery.

METHODS

Outcomes

DED prevalence after cataract surgery was assessed by reviewing systematically evaluated and characterized studies focusing on risk factors, duration, treatment, and DED management after cataract surgery. From the relevant studies, we extracted pre- and postoperative results of DED examinations, including Ocular Surface Disease Index (OSDI) [10–12], tear film breakup time (TFBUT), Schirmer's I test, corneal

fluorescein staining (CFS), tear meniscus height (TMH), tear osmolarity values (TOV) [13], severity peak, and postoperative disease duration. In reports of multiple severity peaks regarding different parameters, the parameter with the most peaks was chosen. Priority was given to subjective symptoms (i.e., OSDI) for any inter-parameter differences.

Search Strategy

We retrieved all articles published between January 1, 2011 and June 9, 2020 by combining the search terms [cataract AND (dry eye) NOT (review)] in key electronic bibliographic databases (PubMed, EMBASE). The search was conducted in June 2020. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses reporting guidelines [14]. Table 1 presents the inclusion and exclusion criteria. The search results were compiled using EndNote X9.3.2 software (Clarivate Analytics, Philadelphia). To maintain the quality standards for reporting systematic reviews and meta-analyses of observational studies [15], the retrieved articles were screened by two researchers (M.M. and T.I.) who independently assessed eligible full-text articles through consensus.

Data Extraction

Two independent reviewers (M.M. and T.I.) extracted the data from eligible articles using standardized data extraction sheets and then cross-checked the results. Inter-reviewer disagreements were resolved through discussions with a third reviewer (J.S.). The following data were extracted: first author name, publication date, study type, country, sample size, follow-up time after cataract surgery, and definition of DED. The following characteristics were assessed in patients with DED after cataract surgery: age, sex, ocular findings, DED prevalence, peak of DED severity, and duration of DED after cataract surgery. Ocular findings were assessed on the basis of the OSDI, TFBUT, CFS, Schirmer's I test, TMH, TOV, and presence of meibomian gland dysfunction (MGD). Figure 1a

Table 1 Study inclusion and exclusion criteria

Inclusion criteria

- Population: Patients who underwent cataract surgery
- Study design: Retrospective studies (cross-sectional and case-control studies) and prospective studies
- Outcomes: Assessment of at least one of the following outcomes: prevalence of DED after cataract surgery, TFBUT, TMH, Schirmer's I test, CFS, TOV, and MGD presence
- Procedures: The procedure was either phacoemulsification or femtosecond laser-assisted cataract surgery

Exclusion criteria

- Clinical guidelines, consensus documents, reviews, systematic reviews, and conference proceedings
- Patients with a history of ophthalmic surgery or ocular surface disorders
- History of intracapsular or extracapsular cataract extraction
- Animal-based studies
- Preprinted articles
- Conference abstracts

CFS corneal fluorescein staining, *DED* dry eye disease, *MGD* meibomian gland dysfunction, *TFBUT* tear film breakup time, *TMH* tear meniscus height, *TOV* tear osmolarity values

summarizes the selection process used for identifying the published studies.

Statistical Analyses

Study-specific estimates (prevalence rates of DED after cataract surgery) were combined through one-group meta-analysis in a random-effects model using OpenMetaAnalyst version 12.11.14 (available from <http://www.cebm.brown.edu/openmeta/>) [16]. Subgroup analyses were performed using studies that reported on each specific outcome.

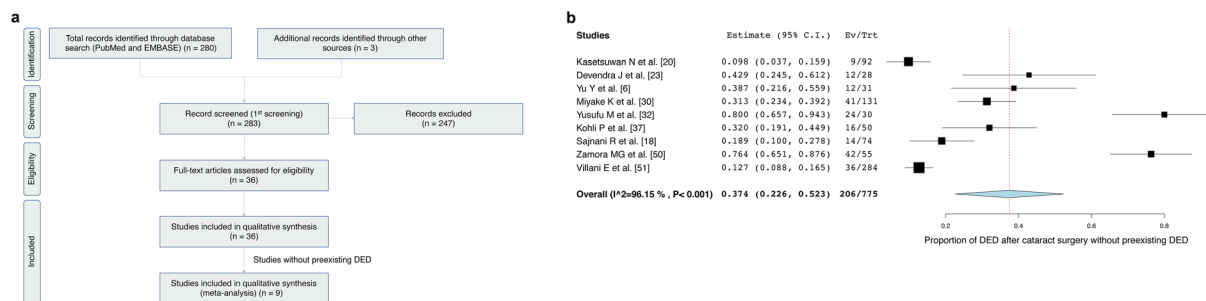


Fig. 1 a Flowchart of the systematic review—PRISMA flow diagram. **b** DED prevalence after cataract surgery. Forest plot of the prevalence rates of DED after cataract surgery in patients without preexisting DED. For each

study, the symbol size corresponds to the sample size. *DED* dry eye disease, *PRISMA* Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Ethics

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

RESULTS

The database search identified 280 articles (Fig. 1a). Three additional articles were selected from the reference lists of the included articles [17–19] and reviewed on the basis of their title and abstract. A total of 247 articles were excluded because of low relevance or article type (clinical guidelines, consensus documents, reviews, systematic reviews, and conference proceedings). Finally, 36 articles were included in the systematic review, nine of which were included in the meta-analysis to estimate the prevalence of DED after cataract surgery in patients without preexisting DED.

Study Characteristics and Demographic Features

Table 2 presents the results of the included studies that were published between November 12, 2013, and June 3, 2020. The details include study type, country, sample size, follow-up time after cataract surgery, definition of DED, and DED-related clinical metrics such as OSDI and TFBUT.

DED Prevalence After Cataract Surgery

Table 2 presents DED prevalence in patients without preexisting DED. Among 775 patients without preexisting DED in nine identified studies [6, 18, 20, 23, 30, 32, 37, 50, 51], 206 (26.6%) individuals developed DED after cataract surgery.

A one-group meta-analysis of the nine studies reporting on DED prevalence after cataract surgery [6, 18, 20, 23, 30, 32, 37, 50, 51] yielded a 37.4% prevalence rate (206/775; 95% CI 22.6–52.3; Fig. 1b).

Severity Peak and Duration of DED After Cataract Surgery

Table 2 summarizes the severity peak and duration of DED after cataract surgery. Although early postoperative ocular surface changes began to recover within a month of cataract surgery [38], most studies reported that DED parameters, including subjective symptoms, TFBUT, CFS, tear secretion volume, and MGD, did not recover to baseline values by the end of the study, indicated as “> (study period).” The peaks of DED severity usually occurred 1 week after cataract surgery, although the reported values ranged from 1 month to more than 1 year [6, 17, 19–23, 26, 27, 29–35, 37, 40, 41, 44, 57, 58]. Notably, eight out of the 22 articles that reported severity peak at 1 month

Table 2 Characteristics of the included studies

Source	Publication date	Study type	Country	Sample size	Follow-up time after cataract surgery	Age, mean ± SD	Sex (F/M)	Definition of DED	Preexisting DED (%)
Kasetsuwan et al. [20]	November 2013	Prospective, descriptive study	Thailand	92 (92 eyes)	3 M	67.2 ± 8.3	61/31	OSDI > 25	0/92 (0)
Han et al. [21]	June 2014	Prospective, observational, case series	Korea	48 (58 eyes)	3 M	68.3 ± 11.7	27/31	NA	NA
Jee et al. [22]	April 2015	Randomized, controlled study	Korea	80 (80 eyes)	2 M	68.6 ± 8.5	53/27	NA	58/58 (100)
Cetinkaya et al. [17]	June 2015	Retrospective study	Turkey	96 (192 eyes)	2.4 M	68.5 ± 8.1	132/60	NA	192/192 (100)
Devendra et al. [23]	October 2015	Single-center, prospective, randomized, controlled trial with a concurrent parallel design	India	58 (58 eyes)	2 M	59.6	28/30	Mild symptoms of DED based on OSDI	0/58 (0)
Sahu et al. [19]	October 2015	Prospective, observational study	India	100 (100 eyes)	2 M	60.8 ± 5.9	59/41	NA	0/100 (0)
Yu et al. [6]	December 2015	Prospective, consecutive, nonrandomized, comparative, cohort study	China	137 (137 eyes)	1 M	71.8 ± 10.1	76/61	The Japanese diagnostic criteria 2006 [24]	72/137 (52.6)
González-Mesa et al. [25]	October 2016	Prospective, observational, cohort study	Spain	52 (52 eyes)	3 M	71.2 ± 8.1	24/28	NA	NA
Kim et al. [26]	September 2016	Prospective, observational, case series	Korea	43 (43 eyes)	3 M	65.0 ± 13.8	13/30	NA	43/43 (100)
Park et al. [27]	October 2016	Prospective, observational study	Korea	34 (48 eyes)	2 M	64.2 ± 6.0	21/27	The DEWS diagnostic criteria 2007 [28]	18/34 (52.9)
Lee et al. [29]	February 2017	Retrospective, comparative, observational, case series	Korea	64 (64 eyes)	3 M	66.7 ± 9.0	45/19	The DEWS diagnostic criteria 2007 [28]	64/64 (100)

Table 2 continued

Source	Publication date	Study type	Country	Sample size	Follow-up time after cataract surgery	Age, mean \pm SD	Sex (F/M)	Definition of DED	Preexisting DED (%)
Miyake et al. [30]	May 2017	Two consecutive prospective study phases (1) Observational study from before cataract surgery to four weeks after surgery (2) Randomized open-label study from 4 to 8 postoperative weeks	Japan	433 (433 eyes)	2 M	71.9 \pm 7.5	234/199	The Japanese diagnostic criteria 2006 [24]	302/433 (69.7)
Kato et al. [31]	September 2017	Randomized, clinical trial	Japan	65 (65 eyes)	2 M	71.8 \pm 7.7	37/28	NA	0/65 (0)
Yusufi et al. [32]	July 2017	Prospective, interventional, case series	China	44 (60 eyes)	1 M	68.7 \pm 2.3	31/29	The TFOS DEWS diagnostic criteria 2007 [28]	8/60 (13.3)
Cui et al. [33]	August 2017	Prospective, open-label, randomized study	Korea	94 (94 eyes)	3 M	63.4 \pm 15.8	60/34	Based on OSDI for over 6 months, TFBUt less than 10 s, Schirmer's test score less than 10 mm per 5 min, and the presence of corneal damage	94/94 (100)
He et al. [34]	December 2017	Prospective, parallel-design, continuous, randomized, controlled study	China	149 (149 eyes)	1 M	69.2 \pm 9.7	94/55	The Chinese Medical Association Ophthalmology Group diagnostic criteria 2013	95/149 (63.8)
Choi et al. [35]	June 2018	Prospective, observational study	Korea	116 (116 eyes)	3 M	66.3 \pm 10.7	62/54	OSDI > 12 [36]	NA
Kohli et al. [37]	June 2018	Prospective study	India	50 (50 eyes)	6 w	60.6 \pm 8.4	26/24	The ODISEY European Consensus Group diagnostic criteria 2014 [38]	0/50 (0)
Sajani et al. [18]	December, 2018	Prospective cohort	USA	119 (119 eyes)	6 M	72 (7.8)	66/53	Dry Eye Questionnaire-5 score \geq 6 [39]	0/119 (0)

Table 2 continued

Source	Publication date	Study type	Country	Sample size	Follow-up time after cataract surgery	Age, mean ± SD	Sex (F/M)	Definition of DED	Preexisting DED (%)
Shao et al. [40]	October 2018	Prospective, single-center, randomized trial	China	233 (300 eyes)	3 M	69.1 ± 12.6	171/129	Schirmer's I test ≤ 10 mm, TF BUT ≤ 5 s, CFS ≥ 1, symptoms, such as dryness, foreign body sensation and burning sensation	0/300 (0)
Nronti et al. [41]	February 2019	Prospective, multicenter, randomized trial	Greece	180 (180 eyes)	6 w	72.7 ± 8.3	98/82	NA	NA
Elksnis et al. [42]	September 2018	Prospective study	Larvia	37 (74 eyes)	1 M	73.1 ± 12.0	21/16	NA	0/37 (0)
Song et al. [43]	April 2019	Prospective, randomized, clinical trial	China	106 (106 eyes)	3 M	63.2 ± 5.0	50/56	NA	106/106 (100)
Ju et al. [44]	July 2019	Single-center, observational study	China	38 (38 eyes)	3 M	72.6 ± 8.7	22/16	The Chinese Medical Association Ophthalmology Group diagnostic criteria 2013	0/38 (0)
Caretti et al. [45]	March 2019	Prospective, randomized, case-control study Randomized, double-blind approach	Italy	60 (60 eyes)	1 M	NA	NA	NA	60/60 (100)
Jun et al. [46]	September 2019	Prospective, randomized, controlled, clinical trial	Korea	117 (117 eyes)	3 M	68.0 ± 7.6	75/42	The TFOS DEWS II diagnostic criteria 2017 [47]	117/117 (100)
Yoon et al. [48]	October 2019	Prospective, randomized, controlled, clinical trial	Korea	24 (24 eyes)	1 M	50–75	NA	The Korean guidelines for the diagnosis and management of dry eye 2014 [49]	24/24 (100)
Zamora et al. [50]	January 2020	Prospective interventional study	Spain	55 (55 eyes)	1 M	75.8 ± 7.3	NA	OSDI > 14.2	0/55 (0)

Table 2 continued

Source	Publication date	Study type	Country	Sample size	Follow-up time after cataract surgery	Age, mean \pm SD	Sex (F/M)	Definition of DED	Preexisting DED (%)
Villani et al. [51]	December, 2019	Single-center, observational, longitudinal study	Italy	284 (284 eyes)	3 M	74.5 \pm 8.2	179/105	The TFOS DEWS II diagnostic criteria 2017 [47]	0/284 (0)
Qiu et al. [52]	January 2020	Prospective study	China	115 (115 eyes)	1 M	65.3 \pm 19.2	53/62	NA	57/115 (49.6%)
Shokoohi-Rad et al. [53]	Februar 2020	Randomized triple-blind clinical trial	Iran	62 (62 eyes)	1 M	64.6 \pm 12.9	18/16	NA	NA
Fognolo et al. [54]	March 2020	Multicenter, pre-marketing, open-label, randomized, prospective study	Italy	45 (45 eyes)	2 w	74 \pm 8	30/15	TFBUT \leq 7 and Schirmer test \leq 15 mm/5 min	NA
Hanyuda et al. [55]	April 2020	Cross-sectional, observational study	Japan	89 (89 eyes)	> 12 M	69.3 \pm 10.4	57/32	The Japanese diagnostic criteria 2006 [24]	NA
Shimabukuro et al. [56]	June 2020	Prospective, observational, case-control study	Japan	67 (67 eyes)	3 M	75.9 \pm 8.3	41/26	The Japanese diagnostic criteria 2006 [24]	48/67 (71.6)

Table 2 continued

Source	Dry eye examinations											
	OSDI		TFBUT		CFS		Schirmer I		TMH		TOV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Kaetsuwan et al. [20]	12.6	33.9	12.2	4.6	The Oxford schema, mean grade I	The Oxford schema, mean grade II	14.1	7.57	NA	NA	NA	NA
Han et al. [21]	NA	NA	6.7 ± 3.0	4.2 ± 1.9	0.4 ± 0.8	0.4 ± 0.7	10.0 ± 3.8	10.0 ± 0.7	NA	NA	NA	NA
Jee et al. [22]	19.5 ± 7.8	17.2 ± 7.0	3.6 ± 1.5	39.0 ± 1.6	1.5 ± 0.5	1.3 ± 0.4	4.2 ± 1.0	4.4 ± 1.1	NA	NA	NA	NA
Cerinkaya et al. [17]	11.7 ± 2.3	7.0 ± 1.0	11.7 ± 2.3	7.0 ± 1.0	NA	NA	6.4 ± 1.4	4.5 ± 1.0	NA	NA	NA	NA
Devendra et al. [23]	NA	NA	12.6 ± 1.7	11.2 ± 1.6	NA	NA	24.6 ± 6.5	24.1 ± 6.4	NA	NA	NA	NA
Sahu et al. [19]	NA	NA	16.1 ± 2.6	9.4 ± 2.6	0.8 ± 0.5	0.8 ± 0.5	17.6 ± 6.9	8.3 ± 6.7	0.4 ± 0.0	0.3 ± 0.1	NA	NA
Yu et al. [6]	23.7 ± 5.8	8.8 ± 4.9	5.0 ± 2.8	4.6 ± 4.0	0.4 ± 0.5	0.7 ± 0.6	9.4 ± 7.4	7.3 ± 6.3	0.2 ± 0.1	0.3 ± 0.1	NA	NA
González-Mesa et al. [25]	33.6 ± 19.6	16.5 ± 16.4	NA	NA	0.0 ± 0.2	0.1 ± 0.4	NA	NA	NA	NA	NA	NA
Kim et al. [26]	25.6 ± 12.0	39.0 ± 10.1	5.8 ± 1.9	3.8 ± 1.0	1.1 ± 0.8	1.4 ± 1.0	9.7 ± 3.4	8.5 ± 2.4	NA	NA	NA	NA
Park et al. [27]	NA	NA	4.2 ± 0.4	3.7 ± 0.5	1.5 ± 0.4	2.1 ± 0.8	5.1 ± 0.5	4.3 ± 0.5	NA	NA	NA	NA
Lee et al. [29]	34.5 ± 21.7	31.7 ± 16.2	4.0 ± 1.3	4.5 ± 2.2	1.0 ± 0.8	0.7 ± 0.8	9.9 ± 3.4	9.6 ± 3.4	NA	NA	NA	NA
Miyake et al. [30]	NA	NA	7.0 ± 2.6	5.7 ± 3.0	1.5 ± 1.4	1.6 ± 1.3	11.8 ± 9.0	12.3 ± 9.9	NA	NA	NA	NA
Kato et al. [31]	NA	NA	7.4 ± 2.7	NA	NA	NA	NA	NA	NA	NA	NA	NA
Yusufu et al. [32]	8.8 ± 10.0	26.9 ± 13.6	9.2 ± 6.5	5.4 ± 2.6	0.5 ± 1.1	1.9 ± 1.9	12.7 ± 6.0	7.2 ± 3.6	0.3 ± 0.1	0.3 ± 0.1	NA	NA

Table 2 continued

Source	Dry eye examinations											
	OSDI		TFBUT		CFS		Schirmer I		TMH		TOV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cui et al. [33]	23.6 ± 3.6	40.4 ± 6.7	5.4 ± 2.6	4.3 ± 2.2	NA	NA	6.1 ± 3.7	4.8 ± 3.5	NA	NA	NA	NA
He et al. [34]	16.8 ± 2.0	NA	NA	NA	NA	NA	13.4 ± 9.3	12.9 ± 9.1	NA	NA	NA	NA
Choi et al. [35]	14.8 ± 15.4	13.1 ± 15.3	5.4 ± 2.1	5.3 ± 2.2	1.2 ± 1.2	0.7 ± 1.0	9.4 ± 4.9	9.5 ± 4.9	NA	NA	NA	NA
Kohli et al. [37]	12.9 ± 4.7	31.3 ± 9.2	11.6 ± 1.0	7.5 ± 2.5	0	2.5 ± 1.0	16.9 ± 2.0	10.6 ± 2.4	NA	NA	NA	NA
Sajani et al. [18]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Shao et al. [40]	0.5 ± 0.4	3.5 ± 0.6	11.0 ± 1.2	8.1 ± 1.1	0.4 ± 0.2	1.0 ± 0.2	9.4 ± 4.0	7.2 ± 3.3	0.4 ± 0.1	0.2 ± 0.1	NA	NA
Nronti et al. [41]	NA	NA	11.5 ± 7.1	11.0 ± 6.8	NA	NA	11.6 ± 3.4	11.9 ± 3.5	NA	NA	NA	NA
Elksnis et al. [42]	NA	NA	NA	NA	NA	NA	13.4 ± 10.5	15.8 ± 9.4	NA	NA	301.2 ± 15.1	311.8 ± 14.9
Song et al. [43]	NA	NA	4.4 ± 1.2	1.2 ± 1.0	0.6 ± 0.7	1.3 ± 1.0	NA	6.6 ± 2.1	NA	NA	NA	NA
Ju et al. [44]	8.4 ± 2.1	17.5 ± 5.5	10.7 ± 1.2	8.1 ± 1.2	0.9 ± 0.7	4.1 ± 1.2	12.9 ± 3.2	13.4 ± 2.6	0.3 ± 0.1	0.4 ± 0.1	NA	NA
Caretti et al. [45]	21.0 ± 12.8	14.4 ± 12.9	4.1 ± 1.6	4.8 ± 1.7	0.7 ± 0.5	0.4 ± 0.4	NA	NA	NA	NA	NA	NA
Jun et al. [46]	22.3 ± 9.0	21.3 ± 12.6	4.6 ± 1.8	3.7 ± 1.4	0.8 ± 0.6	0.3 ± 0.5	11.5 ± 7.6	10.6 ± 6.1	NA	NA	NA	NA
Yoon et al. [48]	27.1 ± 17.2	13.5 ± 6.6	3.1 ± 2.2	3.3 ± 1.9	0.3 ± 0.4	0.2 ± 0.4	NA	NA	NA	NA	295.4 ± 12.1	292.5 ± 11.0
Zamora et al. [50]	11.0 ± 5.1	15.9 ± 6.6	8.8 ± 3.0	6.6 ± 2.7	2.1 ± 1.7	1.1 ± 1.1	9.1 ± 3.6	8.2 ± 2.9	NA	NA	NA	NA
Villani et al. [51]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Table 2 continued

Source	Dry eye examinations											
	OSDI		TFBUT		CFS		Schirmer I		TMH		TOV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Qiu et al. [52]	NA	NA	12.11	5.0	0	1.5	12.9 ± 4.8	20.5 ± 9.7	NA	NA	NA	NA
Shokoohi-Rad et al. [53]	18.0 ± 17.2	20.8 ± 19.6	NA	NA	NA	NA	NA	NA	Meniscometry 5.4 ± 2.4	4.9 ± 2.2	NA	NA
Fognolo et al. [54]	14 ± 8	16 ± 12	7.8 ± 0.7	6.0 ± 1.3	NA	NA	18 ± 5	16 ± 8	NA	NA	305 ± 17	306 ± 17
Hanyuda et al. [55]	NA	NA	4.1 ± 1.7	3.8 ± 1.9	0.2 ± 0.5	0.2 ± 0.6	NA	NA	NA	NA	NA	NA
Shimabukuro et al. [56]	NA	NA	5.7 ± 2.7	NA	0.6 ± 1.6	NA	8.3 ± 6.2	NA	NA	NA	NA	NA

Source	DED prevalence after cataract surgery without preexisting DED (%)		Peak of severity		Duration of DED
	Pre	Post	Pre	Post	
Kasetsuwan et al. [20]	9/92 (9.8)	NA	1 w	NA	> 3 M
Han et al. [21]	NA	NA	3 M	NA	3 M
Jee et al. [22]	NA	NA	1 M	NA	> 2 M
Cetinkaya et al. [17]	NA	NA	1w	NA	3 M
Devendra et al. [23]	12/28 (42.9)	NA	> 2 M	NA	> 2 M
Sahu et al. [19]	NA	NA	10 d	NA	> 2 M
Yu et al. [6]	12/31 (38.7)	NA	1 w	NA	> 1 M
González-Mesa et al. [25]	NA	NA	NA	NA	NA
Kim et al. [26]	NA	NA	1 M	NA	> 3 M
Park et al. [27]	NA	NA	1 d	NA	> 2 M
Lee et al. [29]	NA	NA	1 M	NA	> 3 M
Miyake et al. [30]	41/131 (31.3)	NA	1 M	NA	> 2 M
Kato et al. [31]	NA	NA	1 M	NA	> 2 M
Yusufti et al. [32]	24/30 (80.0)	NA	1 w	NA	> 1 M

Table 2 continued

Source	DED prevalence after cataract surgery without preexisting DED (%)	Peak of severity	Duration of DED
Cui et al. [33]	NA	1 w	> 3 M
He et al. [34]	NA	1 d	> 1 M
Choi et al. [35]	NA	1 M	> 3 M
Kohli et al. [37]	16/50 (32.0)	2 w	> 6 w
Sajani et al. [18]	14/74 (18.9)	NA	> 6 M
Shao et al. [40]	NA	1 w	> 3 M
Ntronti et al. [41]	NA	1 w	> 6 w
Elksnis et al. [42]	NA	1 d	> 1 M
Song et al. [43]	NA	1 M	> 3 M
Ju et al. [44]	NA	1 w	> 3 M
Caretti et al. [45]	NA	1 w	> 1 M
Jun et al. [46]	NA	1 M	> 3 M
Yoon et al. [48]	NA	1 w	> 1 M
Zamora et al. [50]	42/55 (76.3)	1 d	> 1 M
Villani et al. [51]	36/284 (12.7)	3 M	> 3 M
Qiu et al. [52]	NA	1 w	> 1 M
Shokoohi-Rad et al. [53]	NA	1 w	> 1 M
Fognolo et al. [54]	NA	1 w	> 2 w
Hanyuda et al. [55]	NA	NA	> 12 M
Shimabukuro et al. [56]	NA	1 M	> 3 M

CFS, corneal fluorescein staining; DED, dry eye disease; F, female; M, male; NA, not applicable; NEI-VFQ25, National Eye Institute Visual Function Questionnaire; OSDI, Ocular Surface Disease Index, postoperative; pre, preoperative; TFBUT, tear film breakup time; TMH, tear meniscus height; TOV, tear osmolarity values; d, day; w, week; M, month

postoperatively had their first measurement at 1 month [22, 26, 29–31, 35, 43, 46]. Several studies showed varying persistence of DED and ocular surface abnormalities ranging from 2 week to 12 months after cataract surgery [17, 18, 20,

21, 26, 29, 33, 35, 40, 44, 46, 51, 55, 56, 58], possibly preceded by a higher than baseline OSDI, short TFBUT, and MGD at 1 month postoperatively [35]. Corneal denervation or a higher TFBUT score induced by cataract surgery returned to baseline levels within 1–3 months of surgery [17, 59]. Jun et al. [46] reported that preservative-free diquafosol showed better efficacy regarding meibum quality at 1 and 3 months after cataract surgery than preservative-containing diquafosol or preservative-free hyaluronate.

Risk Factors for, Prevention, and Treatment of DED After Cataract Surgery

Accurately recognizing the individual risk factors and initiating perioperative intervention is critical for patients with preexisting DED, particularly for those with minimal signs or symptoms. This section discusses the reported risk factors (Table 3) and prevention/intervention strategies (Table 4) for DED after cataract surgery.

Age, Sex, and Lifestyle

Older age and female sex were associated with DED after cataract surgery [18, 25, 30, 34, 37, 55]. Notably, Kohli et al. [37] showed that individuals above the age of 60 years had worse OSDI, Schirmer test results, TFBUT, CFS, and TMH at 2 weeks post-cataract surgery. Prolonged exposure to visual display terminals, particularly in developed countries, is of concern for the increasing global DED prevalence [61–66]. Villani et al. [51] suggested that the use of computers might exacerbate DED after cataract surgery, advising minimal visual display terminal use during recovery.

Comorbidities: Systemic Diseases, Systemic Medications, and Psychiatric Conditions

The association between DED after cataract surgery and diabetes mellitus was reported [51]. Sajnani et al. [18] evaluated the epidemiology of persistent postsurgical pain (PPP), which manifested as DED-like symptoms for 6 months postoperatively. Autoimmune disorders, non-ocular chronic pain disorder, and use of anti-histamines, anti-reflux medication, antidepressants, anxiolytics, and anti-insomnia medication were reported as risk factors for PPP; hormone replacement therapy, thyroid malfunction, psychiatric conditions, and systemic medication were also reported as risk factors for postoperative DED [51].

Preexisting DED

Two studies [27, 50] reported correlations between preexisting DED and DED after cataract surgery. These studies suggest that preexisting DED may lead to more severe DED postoperatively. Traditional DED metrics that may predict DED after cataract surgery included TFBUT [30, 35, 51], higher CFS [30, 51], conjunctivochalasis [51], Schirmer's I test score [51], and TOV [25]. Additionally, the Ocular Surface Frailty Index (OSFI), developed for DED symptom-onset after cataract surgery [51], might aid in predicting ocular surface symptoms with $OSFI \geq 0.3$. Lid-parallel conjunctival folds and ocular allergy predicted DED to some extent [51].

MGD

MGD affects tear-film stability and is strongly associated with DED [67]; the accelerated tear-evaporation rate and the subsequent tear hyperhidrosis in MGD likely trigger DED development [35, 43, 51, 52, 68]. Clinically, this is observed as MGD aggravated by cataract surgery, with a positive correlation between MGD and DED-related indicators including postoperative TFBUT and CFS [52]. Conversely, a Chinese trial [43] has shown that preoperative MGD management might allow effective and optimal alleviation of obstructive-MGD and DED induced by cataract surgery.

Table 3 Risk factors for DED after cataract surgery

Risk factor	Country	Year	Sample size	Adjusted odds ratio (95% CI)	References
Age					
Older	India	2018	50 (50 eyes)	NA	Kohli et al. [37]
	Japan	2020	86 (86 eyes)	1.02 (0.97–1.06)	Hanyuda et al. [55]
Sex					
Female	Spain	2016	52 (52 eyes)	NA	González-Mesa et al. [25]
	China	2017	149 (149 eyes)	NA	He et al. [34]
	Japan	2017	433 (433 eyes)	3.15 (2.12–4.67)	Miyake et al. [30]
	USA	2018	119 (119 eyes)	2.68 (1.20–6.00)	Sajnani et al. [18]
	Japan	2020	86 (86 eyes)	2.90 (1.18–7.17)	Hanyuda et al. [55]
Systemic diseases					
Autoimmune disorder	USA	2018	119 (119 eyes)	13.2 (1.53–114)	Sajnani et al. [18]
Diabetes	Italy	2020	284 (284 eyes)	1.12 (1.37–7.11)	Villani et al. [51]
Hormone replacement therapy	Italy	2020	284 (284 eyes)	3.36 (2.18–8.29)	Villani et al. [51]
Non-ocular chronic pain disorder	USA	2018	119 (119 eyes)	4.29 (1.01–18.1)	Sajnani et al. [18]
Thyroid malfunction	Italy	2020	284 (284 eyes)	1.65 (1.30–6.99)	Villani et al. [51]
Systemic medications					
Antihistamine	USA	2018	119 (119 eyes)	6.22 (2.17–17.8)	Sajnani et al. [18]
Anti-reflux medication	USA	2018	119 (119 eyes)	2.42 (1.04–5.66)	Sajnani et al. [18]
Systemic medications	Italy	2020	284 (284 eyes)	1.70 (0.17–4.83)	Villani et al. [51]
Psychiatric conditions					
Anxiolytic use	USA	2018	119 (119 eyes)	3.38 (1.11–10.3)	Sajnani et al. [18]
Antidepressant use				3.17 (1.31–7.68)	
Anti-insomnia medication use				5.28 (0.98–28.5)	
Psychiatric conditions	Italy	2020	284 (284 eyes)	2.25 (0.98–6.25)	Villani et al. [51]

Table 3 continued

Risk factor	Country	Year	Sample size	Adjusted odds ratio (95% CI)	References
Preexisting DED	Korea	2016	34 (48 eyes)	NA	Park et al. [27]
	Spain	2020	55 (55 eyes)	NA	Zamora et al. [50]
Short TFBUT	Japan	2017	433 (433 eyes)	3.96 (2.59–6.06)	Miyake et al. [30]
	Korea	2018	116 (116 eyes)	0.32 (0.18–0.57)	Choi et al. [35]
	Italy	2020	284 (284 eyes)	1.95 (1.08–7.52)	Villani et al. [51]
Higher CFS	Japan	2017	433 (433 eyes)	Score 1 and 2: 2.98 (1.89–4.69) More than score 3: 4.82 (2.78–8.35)	Miyake et al. [30]
	Italy	2020	284 (284 eyes)	1.63 (0.87–7.64)	Villani et al. [51]
Others					
Conjunctivochalasis	Italy	2020	284 (284 eyes)	1.12 (1.37–7.71)	Villani et al. [51]
Higher Schirmer test score				1.21 (1.13–7.00)	
LIPCOF				1.52 (2.04–8.07)	
Ocular allergy				2.22 (0.96–6.63)	
Ocular Surface Frailty Index				9.45 (4.74–18.8)	
TOV \geq 312 mOsm/L	Spain	2016	52 (52 eyes)	NA	González-Mesa et al. [25]
MGD	Korea	2018	116 (116 eyes)	Increased MG dropout: 1.15 (1.04–1.26) Low MG orifice obstruction scores: 0.29 (0.11–0.78)	Choi et al. [35]
	Italy	2020	284 (284 eyes)	1.88 (0.78–5.82)	Villani et al. [51]
	China	2019	106 (106 eyes)	NA	Song et al. [43]
	China	2020	115 (115 eyes)	NA	Qiu et al. [52]
Eye-drop					
NSAID drops	Japan	2017	65 (65 eyes)	NA	Kato et al. [31]
Preservative use	Korea	2015	80 (80 eyes)	NA	Jee et al. [22]
	Korea	2019	117 (117 eyes)	NA	Jun et al. [46]
Topical drugs	Italy	2020	284 (284 eyes)	1.08 (1.06–7.56)	Villani et al. [51]
Surgical techniques					
Increased effective phacoemulsification time	India	2018	50 (50 eyes)	NA	Kohli et al. [37]

Table 3 continued

Risk factor	Country	Year	Sample size	Adjusted odds ratio (95% CI)	References
Femtosecond laser application	China	2015	137 (137 eyes)	NA	Yu et al. [6]
	China	2018	233 (300 eyes)	NA	Shao et al. [40]
	China	2019	38 (38 eyes)	NA	Ju et al. [44]
Increased surgical microscope-light exposure	India	2018	50 (50 eyes)	NA	Kohli et al. [37]
Lifestyle					
Computer use	Italy	2020	284 (284 eyes)	1.90 (0.82–4.34)	Villani et al. [51]

CFS corneal fluorescein staining, *CI* confidence interval, *DED* dry eye disease, *LIPCOF* lid-parallel conjunctival folds, *OSDI* Ocular Surface Disease Index, *MG* meibomian gland, *MGD* meibomian gland dysfunction, *NA* not applicable, *NSAID* non-steroidal anti-inflammatory drug, *TFBUT* tear film breakup time

Preservatives and NSAIDs in Eye Drops

Preservative-containing topical eye drops for intraoperative or postoperative use, including benzalkonium chloride, may cause ocular surface damage stemming from epithelial cell injury and apoptosis and reduced goblet cell density [69, 70]. Jee et al. [22] compared the efficacy of preservative-free versus preservative-containing sodium hyaluronate 0.1% and flurometholone 0.1% eye drops after cataract surgery. The preservative-free group showed superior DED-related metrics, impression cytology findings, goblet cell count, tear interleukin-1 β and tumor necrosis factor- α levels, and catalase and superoxide dismutase levels at 2 months postoperatively. Further, a Korean study reported that compared with preservative-containing diquafosol, preservative-free diquafosol 3% showed better efficacy in treating DED after cataract surgery [46].

Kato et al. [31] observed the negative effects of topical non-steroidal anti-inflammatory drugs (NSAIDs) after cataract surgery on conjunctival goblet cell density, raising concerns about DED with prolonged topical NSAID administration. Interestingly, topical rebamipide, widely used to prevent oral NSAID-induced gastric mucosal damage [71], counteracts the reduction of conjunctival goblet cell density induced by diclofenac [31].

Treatment Selection and Adjuvant Therapies

Artificial tears and sodium hyaluronate 0.1% are common first-line treatments for DED [66, 72]; however, treatments are shifting toward more complex and effective topical drops [73]. Diquafosol tetrasodium solution is reportedly effective for DED treatment after cataract surgery with comparative benefits over artificial tears or sodium hyaluronate 0.1% [29, 30, 33, 46].

Addition of trehalose to sodium hyaluronate also effectively reduces DED symptoms and improves clinical outcomes (TFBUT, OSDI) after cataract surgery, possibly owing to its propensity for deep hydration, lipid and protein stabilization, protection against oxidative insult, and epithelial cell recovery [45]. Fogagnolo et al. [54] reported improvements in TFBUT and OSDI with antioxidant solution usage for 2 weeks pre- and postoperatively, implicating antioxidants in protecting ocular surface homeostasis from surgical invasions. Oral lactoferrin [23] and omega-3 fatty acid [60] (over-the-counter supplements established as effective adjuvants for DED treatment) have also been implicated in the management of DED after cataract surgery.

Surgical Techniques

Increased duration of surgery and longer phacoemulsification time may be risk factors for postoperative DED, compounded by increased

Table 4 Prevention and treatment of DED after cataract surgery

Treatment	Intervention	References
Topical eye drops		
0.2% sodium hyaluronate artificial tears	Postoperative	Ntonti et al. [41]
Antioxidant solution	Postoperative	Fogagnolo et al. [54]
Carbomer sodium hyaluronate trehalose	Postoperative	Caretti et al. [45]
Diquafosol tetrasodium 3%	Postoperative	Cui et al. [33] Miyake et al. [30] Lee et al. [29]
Preservative-free 3% diquafosol	Postoperative	Jun et al. [46]
Preservative-free sodium hyaluronate 0.1% and fluorometholone 0.1%	Postoperative	Jee et al. [22]
Rebamipide	Postoperative	Kato et al. [31]
Preoperative MGD treatment		
Preoperative MGD treatment	Postoperative	Song et al. [43]
Intraoperative and other postoperative treatments		
Hydroxypropyl methylcellulose	Intraoperative	He et al. [34] Yusufu et al. [32]
Ophthalmic viscosurgical device	Intraoperative	Yoon et al. [48]
Oral adjuvant omega-3 fatty acid	Postoperative	Mohammadpour et al. [60]
Oral lactoferrin	Postoperative	Devendra et al. [23]

DED dry eye disease, *MGD* meibomian gland dysfunction

microscopic light exposure [37]. Further, femtosecond laser-assisted cataract surgery is among the reported risk factors for DED after cataract surgery [6, 40, 44, 74], likely owing to peri-conjunctival injury caused by the femtosecond laser suction ring.

These results suggest that light filters, short surgery duration, adequate irrigation, and soft manipulation of the ocular surface tissue may minimize surgery-related complications [20]. Use of an ophthalmic viscosurgical device—normally used to prevent intraocular tissue damage during cataract surgery—on the ocular surface has shown protective effects for a week postoperatively with significant improvements in TFBUT, corneal ocular staining score, and OSDI [48]. Administration of hydroxypropyl methylcellulose on the corneal surface also

results in improved clinical outcomes related to tear film and ocular surface health [32].

DISCUSSION

This is the systematic review and meta-analysis to comprehensively present DED prevalence after cataract surgery that included 775 individuals from nine articles [6, 18, 20, 23, 30, 32, 37, 50, 51]. We observed that 37.4% (95% CI 22.6–52.3; 206/775) of patients without preexisting DED developed DED postoperatively, highlighting the importance of perioperative DED management in addressing postoperative patient dissatisfaction and decreased QOV. The global DED prevalence is 5–50% [75]; inclusion of cataract surgery-

related DED may expand it to half of the global population. Thus, a thorough and effective DED assessment during the perioperative period of cataract surgery is warranted [8, 62].

The major mechanisms underlying DED pathogenesis include tear-film instability and ocular surface inflammation [47, 76–80]. We observed that DED after cataract surgery was weakly and strongly associated with tear secretion (Schirmer's I test) and TFBUT, respectively [22, 29, 30, 35, 44, 52]. Additionally, postoperative upregulation of inflammatory mediators contributes to DED development [27, 77–81], which simultaneously alters subjective perception and sensitivity of the ocular surface nerve plexuses [82]. This might be attributed to the surgical procedure itself and/or preservatives in postsurgical eye drops, both of which contribute to inflammation and tear-film instability [37, 83, 84]. Larger corneal wounds [84], longer microscopic exposure times [21, 37], and greater phacoemulsification energy [37] increase the likelihood of DED after cataract surgery, including the persistent decrease of conjunctival goblet cells despite an uncomplicated phacoemulsification [59, 84].

MGD is closely related to DED pathology [35, 43, 52], and Han et al. [21] reported persistent MGD after cataract surgery without accompanying structural changes even in patients without preexisting MGD. A Japanese study [56] focused on TFBUT patterns in patients with DED after cataract surgery, observing a random break pattern that was predominant during the postoperative period, which is a common feature in evaporative DED and is often associated with MGD [85]. Therefore, owing to potential comorbidity, MGD should be preoperatively evaluated in all patients regardless of preexisting DED [21, 26, 35, 52].

Additionally, we investigated the risk factors for DED after cataract surgery, which were consistent with the characteristics reported by epidemiological studies on DED in the elderly [86]. Patients with traditional DED risk factors [8, 63–65] may present with DED after cataract surgery; therefore, preventative measures should be considered. Other non-ocular risk factors include various systemic diseases,

systemic medications, and psychiatric conditions. Notably, diabetes mellitus is among the systemic risk factors for DED [87], likely affected by tear hyperosmolarity and tear-film instability resulting from dysfunction of lacrimal functional units and the ocular surface. The effects of hyperglycemia on the lacrimal gland functional unit components are systematically transmitted via neural connections, resulting in abnormal tear production and composition, both of which contribute to DED [8]. Ultrasonic energy produced during phacoemulsification can cause free radical formation [88], which may compound the damage. Although the exact underlying mechanisms remain unclear, other systemic diseases and treatments damage the conjunctiva, lacrimal glands, goblet cells, and peripheral nerve innervations, predisposing the affected population to DED after cataract surgery.

There is a recent consensus regarding the concomitant role of neurogenic stress and ocular surface inflammation on DED pathogenesis [8]. Additionally, DED is associated with other chronic pain conditions and may alter the genetic susceptibility for depression [65, 89]. Patients with DED usually present with chronic pain syndromes, which are associated with increased severity of subjective DED symptoms, even with comparable objective ocular surface signs [90]. Anxiety disorders and usage of anxiolytics, antidepressants, or sleep medication are also associated with DED after cataract surgery [18]. Extrapolating the psychogenic effects on ocular sensations, it is possible that only the subjective indicators are elevated for specific populations, although further studies are required to validate the hypothesis. The relationship between surgical techniques and DED after cataract surgery was also analyzed. Studies have reported a correlation of DED examination values with microscopic light exposure time [37] and phacoemulsification energy used [37]; surgeons should strategize to minimize both factors in patients with preoperative DED or risk factors.

Pathological changes and inflammatory kinetics preceding DED after cataract surgery are crucial when determining postoperative treatment and management. DED severity after

cataract surgery tends to peak around 1 week postoperatively [6, 19, 20, 32, 34, 40–42, 44, 45, 52–54]. Notably, numerous studies reported postoperative follow-ups scheduled after 1 week and 1 month, and the true peak of DED symptoms most likely lies within this time period. Kasetsuwan et al. [20] proposed that the timeline of corneal neuron regeneration and DED symptom exacerbation within 1 postoperative month may be correlated. As new neurite cells emerge, there is a stark increase in neural growth factors at 25 days postoperatively, indicative of sub-epithelial corneal axon regeneration. Khanal et al. [91] reported that alterations in corneal neuronal plexuses and a postoperative decrease in the blink rate reduced corneal sensitivity and feedback. Moreover, the authors reported recovery of tear functions within 1 postoperative month, supporting the existence of a DED peak within 1 week and 1 month postoperatively. Notably, this result also coincides with the observed increased tear evaporation up to 1 month postoperatively, associated with usage of benzalkonium chloride preservatives [92].

DED duration after cataract surgery is clinically important. Studies have reported a wide range of DED duration, from 1 months to more than 1 year [17, 18, 20, 21, 26, 29, 33, 35, 40, 44, 46, 51, 55, 56, 58]. Further, some studies have reported that surgery-induced invasive corneal changes recover within 1–3 months [17, 59]. The long-term effects of DED after cataract surgery remain unclear as most patients, particularly after successful bilateral cataract surgery, require follow-up for only a few months. While further studies are needed, the results show that consistent follow-up for DED is necessary for at least 1 month after cataract surgery.

Postoperative eye drops should be carefully selected owing to variable efficacy and the presence of preservatives. Several studies have suggested a correlation between preservatives and DED after cataract surgery [22, 46], advising preservative-free treatment options for surgery recipients. Considering the multifactorial pathophysiology of DED and the wide-ranging effects of cataract surgery on the ocular surface, future strategies for addressing DED after

cataract surgery require surgeons to gain a better understanding of treatment and prevention methods.

This review has several limitations. First, only a few included studies had a follow-up period of more than 1 year, which limited the analysis of long-term effects. Second, approximately three-quarters of the included articles were published in Asian countries, which partially limits the generalizability of the findings. Third, the criteria and dry eye examination techniques for DED diagnosis have not been standardized across countries and practices, and the included studies showed inconsistencies in their diagnostic standards. Future studies should consider further standardization of the diagnostic criteria and generalizability of the study results through the inclusion of participants of different ethnic groups, longer observation periods, and use of standardized guidelines for DED diagnosis, such as those proposed by the Tear Film & Ocular Surface Society [47] and the Asia Dry Eye Society [76].

CONCLUSIONS

This study comprehensively analyzed DED prevalence and characteristics after cataract surgery. It presents a concise and up-to-date description of the risk factors, prevention, and treatments. Our findings contribute to generating increased awareness among physicians, researchers, and the general population regarding DED after cataract surgery and encourage the development of effective preventative and treatment strategies.

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